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Rotavirus species tropism: new insights on P-type classification

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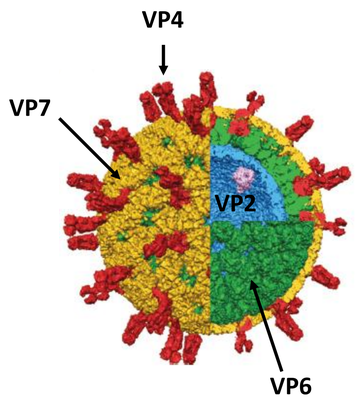
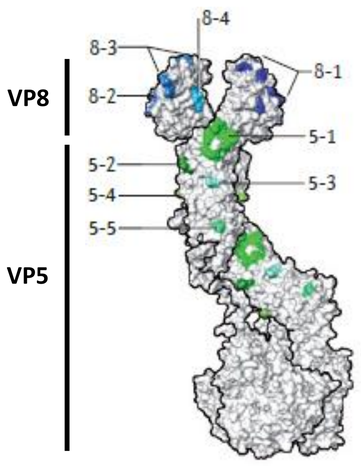
Introduction

- Rotavirus group A (RVA) infects enterocytes of a broad range of species with high specificity between strain and host cells (A).
- VP4 is mainly responsible for virus internalization and cell tropism. To date, 49 P-types (VP4) were reported.
- This protein is composed of two domains VP5 and VP8, which possess a trimer structure in the basal region and a dimer structure in the distal region (spike), with the VP8 domains on the top of the spike (B).
- During the attachment to the cell, a conformational change trigger of the RNA of the virus into the cell (C).



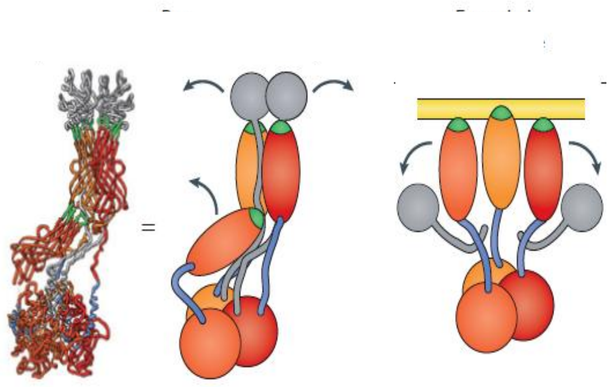
Trask et al, 2012. Current Opinion in Virology, 2:373–379



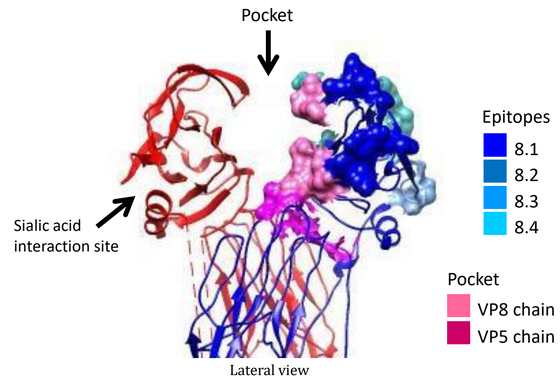
Trask et al, 2012. Nature Review 10: 165-177

Objective

To study the aminoacid regions that are involved in the VP8 pocket in order to find a molecular fingerprint for the virus species tropism.

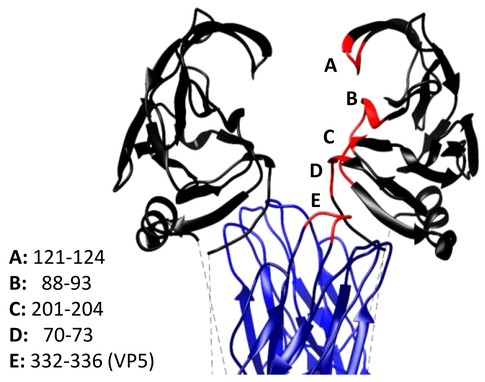


Trask et al, 2012. Nature Review 10: 165-177

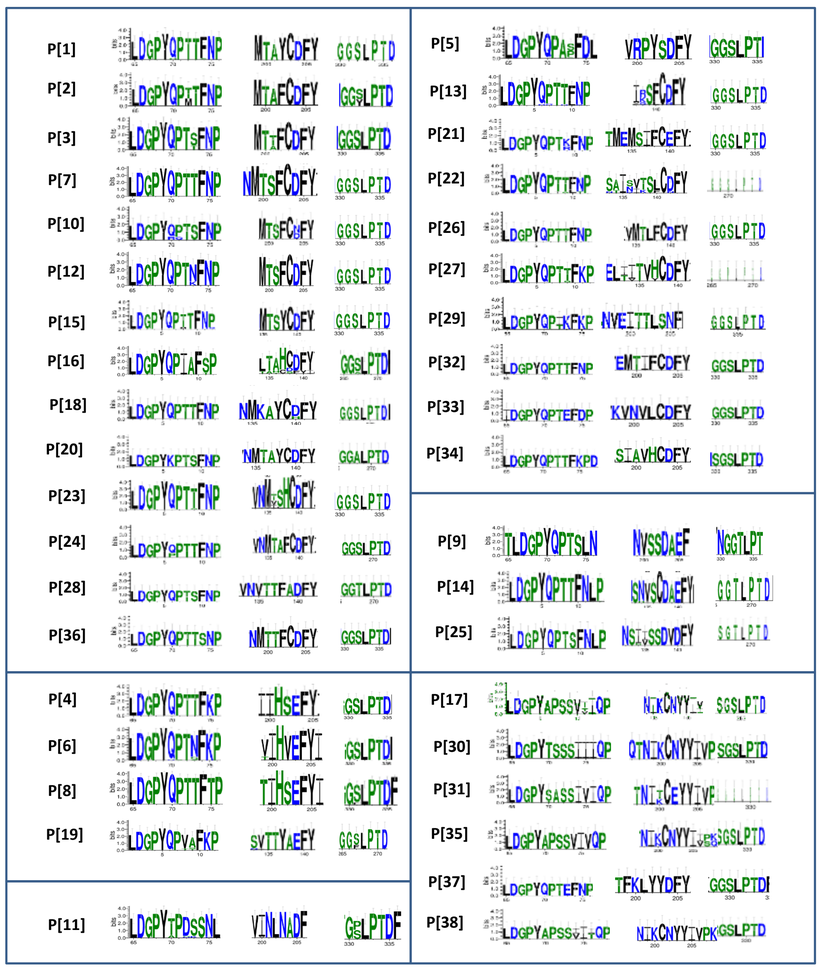


Material and Methods

- All sequences are available at genbank database (https://www.ncbi.nlm.nih.gov/genome/viruses/).
- Alingment were done in ClustalW and the edition were carried out with Bioedit.
- Structural Modeling and Analyses: The molecular modeling was carried out using I-Tasser online server (http://zhanglab.ccmb.med.umich.edu/I-TASSER/), without customizing any template model. Modeling was based on experimentally solved structures from RVA strains. The VP4 trimers, visualization and graphs were reconstructed using the UCSF Chimera package (https://www.cgl.ucsf.edu/chimera/).



P - type	Sequences (n)
P[1]	50
P[2]	12
P[3]	28
P[4]	29
P[5]	120
P[6]	101
P[7]	29
P[8]	>150
P[9]	>150
P[10]	>150
P[11]	42
P[12]	70
P[13]	24
P[14]	35
P[15]	9
P[16]	20
P[17]	5
P[18]	5
P[19]	10
P[21]	3
P[22]	10
P[23]	38
P[24]	3
P[25]	8
P[26]	3
P[27]	7
P[28]	1
P[29]	4
P[30]	7
P[31]	9
P[32]	1
P[33]	1
P[34]	1
P[35]	7
P[36]	4
P[37]	2
P[38]	2
P[39]	1



				72 – 78	121-124	202-207
P[Ia]	Bovine>Human> Porcine>simian> Caprine>equine> Camelid	USA/NCDV/1967/G6	P[1]	TTFNPPV	LFGQ	NMTAYC
	Equine	GBR/L338/1991/G13	P[18]	.....	....	..K...
	Simian	ZAF/SA11-H96/1958/G3	P[2]	.....	I..I	....F.
	Simian>human> Feline>simian> Bovine>caprine	USA/RRV/1975/G3	P[3]	.S.....	...T	....F.
	Simian	USA/TUCH/2002/G3	P[24]	.....T	...V	....F.
	Porcine>bovine>human	USA/OSU/1977/G5	P[7]	.....T	....	...SF.
	Human	IND/69M/1980/G8	P[10]	.S.....	...I	...SF.
	Equine	ARG/E30/1993/G3	P[12]	.K.....	...V	T..SF.
	Porcine	Pig-wt/VEN/A34/2002/Gx	P[23]	.....	...H	..VSH.
	Ovine>bovine	XXX/LP14/XXXX/G10	P[15]	M...Q..	...E	...S..
	Mouse	USA/EW/XXXX/G16	P[16]	IA.S..P	...I	.L..H.
	Mouse	XXX/EHP/1981/G16	P[20]	.S....T	I..S	.....
	Human	ECU/Ecu534/2006/G20	P[28]	.S....I	...S	.V.TFA
P[Ib]	Human	IND/HP140/1987/G6	P[13]	TTFNPPI	IFGQ	EIRSFC
	Rabbit	ITA/160/2001/G3	P[22]	.....	....	NVT.L.
	Porcine	ITA/134-04-15/2003/G5	P[26]	.....	....	VMTL..
	Porcine	IRL/61-07-ire/2007/G2	P[32]	V	V..E	.MTI..
	Bovine	IND/HG18/1995/G15	P[21]	.R...E.	...K	.MSI..
	Bovine	JPN/Dai-10/2007/G24	P[33]	.E.D...	...K	KVNVL.
	Bovine	GBR/UK/1973/G6	P[5]	AP.DL.V	M..S	.V.PYS
	Porcine	THA/CMP034/2000/G2	P[27]	...K.DV	L..K	I.TVH.
	Porcine	JPN/FGP51/2009/G4	P[34]	...K.DV	L...	S.AVH.
	Bovine	JPN/Azuk-1/2006/G21	P[29]	IK.K.DN	.YDE	..TTLS
P[II]	Human	USA/DS-1/1976/G2	P[4]	TTFKPPN	LFGE	SIIIHS
	Human	USA/WA/1974/G1	P[8]	...T...	I...	..T...
	Human>porcine	BGD/Dhaka12/2003/G12	P[6]	.N.....	....	ETV..V
	Porcine>Human	IND/RMC321/1990/G9	P[19]	VA.....	...V	.VTTYA
P[III]	Human>feline>canine	JPN/AU-1/1982/G3	P[9]	TSLNLPV	LDGQ	NVSSDA
	Human>	ITA/PA169/1988/G6	P[14]	.TF...I	....	...C..
	Human	BGD/Dhaka6/2001/G11	P[25]	..F....	....	II...V
P[IV]	Human	IND/I321/XXXX/G10	P[11]	DSSNLPS	VMNE	VINLNA
P[V]	Pigeon	JPN/PO-13/1983/G18	P[17]	SSVIIQP	ILGR	QTNIKC
	Chicken	DEU/02V0002G3/2002/G19	P[30]	..I....	...H	.....
	Chicken	DEU/06V0661/2006/G19	P[31]	..IV...	...K	....T.
	Turkey	GER/Tu-03V0002E10/Gx	P[35]	....V..	...K	.....

Class	Genotype	Strain	Glycan	Cleft
(A) Human s-l	P[14]	HAL1166	A-HBGA	narrow
	P[9]	KB	A-HBGA	narrow?
(B) Human s-l	P[4]	DS-1	HBGA	wide
	P[8]	Wa	GM1, HBGA	wide
	P[6]	McN13	HBGA?	wide?
	P[11]	N1509	LacNAc	wide?
(C) Animal s-s	P[3]	Simian RRV	Sia	narrow
	P[7]	Porcine CRW8	Sia	narrow
(D) Animal s-l	P[5]	Bovine UK	?	narrow?
	P[12]	Equine H2	?	narrow?
	P[16]	Murine Eb	?	narrow?

Prasad et al, 2014. Curr Op Virol 7: 119-127

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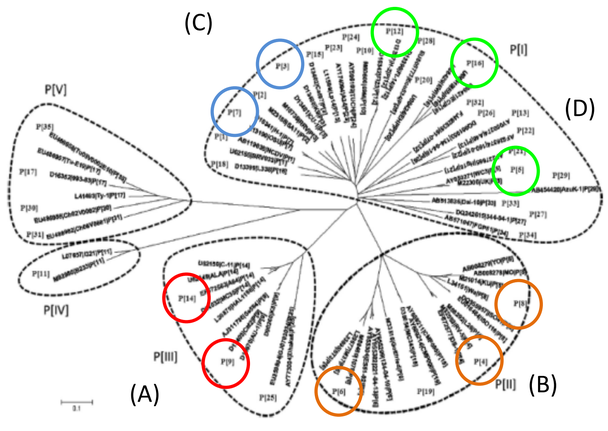

Liu et al, 2012. J Virology 86 (18): 9899-9810

The structure of the Rotavirus spike functions as the ligand of a cell receptor protein with the initial sialic acid dependant interaction located on the external part of the spike. In a second step for cell infection the aminoacids on the spikes pocket interact with another cell receptor which is specific for specie. This correlation between the sequence of the pocket and the host tropism could be useful for taxonomy classification.

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